THE

AMERICAN JOURNAL

OF THE MEDICAL SCIENCES

FOR JANUARY, 1885.

ARTICLE I.

INJECTION OF FINELY POWDERED INORGANIC MATERIAL INTO THE ABDOMINAL CAVITY OF RABBITS DOES NOT INDUCE TUBERCULOSIS. AN EXPERIMENTAL RESEARCH.

By GEORGE M. STERNBERG, Major and Surgeon, U. S. A., WITH PATHOLOGICAL NOTES by WM. T. COUNCILMAN, Associate in Pathology, Johns Hopkins University.

WHEN Koch first announced to the world his discovery of the tubercle bacillus, and gave an account of the experimental evidence which had convinced him of its essential etiological relation to the disease tuberculosis, it was natural that conservative physicians should demand additional evidence and confirmation from other sources before accepting his conclusions, notwithstanding the reputation which he had already established as an expert and conscientious investigator. The special reasons for exercising an unusual degree of scientific scepticism in accepting Koch's account of the etiology of this disease were stated by the writer in the following language in a paper published in *The Medical News*, July 1, 1882:—

> "Koch began this investigation as an *expert*, familiar from long practice with the technique of culture experiments and microscopical investigations with the highest powers. Probably no man living was better fitted by natural aptitude and past experience for carrying out an experimental research of this kind, and certainly very few would have been able to command as great confidence in the result announced in advance of confirmation by other observers. Still this confirmation is necessary in order to establish the discovery of Koch among the demonstrated truths of medical science. This is all the more essential, inasmuch as other observers—Klebs and Toussaint—have found in their experimental researches, organisms, *microccocci*, believed by them to be the agents of tuberculous infection, which differ morphologically from those—*bacilli*—described by Koch; and more especially because it has been demonstrated by repeated experiments that a

disease closely resembling tuberculosis, if not identical with it, may be produced in animals by inoculation with a variety of organic products of non-tubercular origin, and even by the inhalation of inorganic particles. Thus Brunet[1] inoculated seven rabbits with cancer, six with simple pus, and six with tuberculous matter. Of these, fourteen became tuberculous, viz., six of those inoculated with cancer, three of those inoculated with pus, and five of those inoculated with tuberculous matter.

Shottelius[2] found that miliary nodules in the lungs resulted, in dogs, alike from the inhalation of the pulverized—spray—sputum of phthisis and of bronchitis.

Toussaint affirms that the tubercular deposits resulting from inoculation with non-tubercular material are not infectious, and that experimental pseudo-tuberculosis may be distinguished from tuberculosis proper by inoculation experiments, although the pathological anatomy of the two diseases is identical.

If we accept the view that the tubercle nodules are of inflammatory origin, we can readily understand how both living and non-living particles may give rise to local inflammatory processes, resulting in similar pathological products, and the infectious or non-infectious character of these products would then be explained by the presence or absence of living organisms, in accordance with the views of Burdon-Sanderson,[3] who says, '*Whenever an inflammation becomes infectious, it owes that property to chemical change in the exudative liquid, of which the presence of microzymes is a necessary condition.*'

The weight of experimental evidence seems to the writer to favor the view that the specific properties of Koch's bacillus depend upon its ability to locate itself in certain situations, rather than in any power to produce a special kind of inflammation, giving rise to products having specific characters. If this is the case, we should expect that other organisms capable of locating themselves in the same situations would likewise give rise to tubercular neoplasms. In a recent communication to the French Academy of Sciences, we have evidence presented that such is the case.

M. Laulainé,[4] in a note presented by M. Bouley, on the 2d of January of the present year, makes the following statements:—

The author had recently observed in the lungs of a dog the alterations produced by the eggs of a nematoid worm, the *strongylus vasorum* (Baillet), which possess great interest, because of their apparent identity with those of tuberculosis. These *strongyles* in the adult state live in the right ventricle and in the larger divisions of the pulmonary artery. Here they are massed together in balls of greater or less magnitude, which consist of individuals of both sexes. These masses are restrained from being washed away by the blood current by anastomosing fibrous bands, which are developed as the result of an endarteritis, which is infallibly produced by the presence of the parasites. The fertilized eggs emitted by the females in these tangled masses in the central part of the circulation, are carried along by the current to the smallest arteries and capillaries, where they are arrested and where the embryos are born. These emigrate immediately to the smaller bronchial tubes. The lungs of dogs infested with this parasite are filled with fine gray granulations, the histological characters of which are described by the author as follows:—

'The eggs and the embryos arrested in the smallest *arterioles* become the point of departure of a nodular arteritis, presenting in its structure all the characters assigned, since Köster, to the elementary follicles of tuberculosis. At the centre of each nodule is found an egg or an embryo inclosed in a giant cell, this is surrounded by a more or less abundant collection of *epithelioid* cells or by an exterior embryonic zone which tends frequently to become fibrous.'

The author points out that this pseudo-tuberculosis affects especially the base of the pulmonary lobes, differing in this respect from true tuberculosis which is located by preference at the summit.

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[1] Sur la tuberculose expérimental, C. R. A. des Sciences, t. xciii. p. 447.

[2] Experimentelle Untersuchungen über die Wirkung inhalirter Substanzen. Archiv f. Path. Anat. und Phys. lxxiii. p. 524.

[3] The Lumleian Lectures on Inflammation. British Medical Journal, April 15, 1882, p. 527.

[4] Sur une tuberculose parasitaire du chien et sur la pathogénie du follicule tuberculeux. C. R. Ac. des Sci., i. xciv. p. 49.

The present writer intends to repeat the experiments of Koch, if circumstances and the limited facilities now at his command enable him to do so, and if any results are attained worthy of record, proposes to communicate them in a second paper to which this will serve as an introduction."

In attempting to carry out the intention above announced, the writer, being stationed at a military post on the Pacific coast, and depending entirely upon his own resources, met with difficulties which prevented him from completing his self-imposed task. Many minor difficulties were encountered, among which may be mentioned that of obtaining animals for experimental purposes, and the consciousness that public sentiment in the garrison was opposed to experiments of this nature, the importance of which was not appreciated, while exaggerated ideas of the sufferings of the animals were entertained, *especially by the commanding officer's wife.* But the main difficulty encountered resulted from the absence of gas, and of a suitably constructed culture oven, and a consequent failure to obtain cultures of the bacillus after all of the preceding steps in the investigation had been carried out in a successful manner.

The bacillus was found in tuberculous sputum. Rabbits and guinea-pigs were inoculated with sputum of phthisical patients, and characteristic tubercle nodules were found in the lungs and liver as a result of such inoculations; but when these nodules were placed with due precautions upon the surface of sterilized blood serum, prepared as directed by Koch, they remained for weeks without the appearance of any scales made up or bacilli, such as Koch described in his first report and has since represented in the beautiful chromo-lithographs[1] illustrating his recent elaborate memoir published in the second volume of The Report of the Imperial Board of Health of Germany.

This failure to obtain cultures was doubtless due to imperfect regulation of temperature in the improvised culture-chamber, which, in the absence of anything better, I attempted to use, and which answered very well for the cultivation of various other micro-organisms less susceptible to slight variations of temperature.

To repeat the attempt at the present time would be simply a matter ot personal gratification, for the possibility of cultivating the bacillus through successive generations has been demonstrated beyond question, not only by Koch and his assistants, but by Watson Cheyne, of London, and quite recently in our own country by Dr. Ernst, of Massachusetts. I cannot, however, admit that the experiments of the last-named gentleman, detailed in his interesting paper in the October number of this journal, are by themselves convincing as to the essential etiological rôle of the bacillus in the production of tuberculosis; for, in my opinion, considerably more than three successive cultures must be made in order to insure the exclusion of any trace of the original material, especially in the case of an organism, which develops as slowly as does the tubercle bacillus, and which extends but a limited distance from the point of inoculation upon the surface of a solid culture medium.

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[1] The writer has taken the liberty of introducing into the second edition of his work on "Bacteria," a chromo-lithographic plate in which the figures have been accurately copied from some of those above referred to.

But Koch himself has carried these cultures so far, and has multiplied his inoculation experiments with "pure cultures" to such an extent that the experimental evidence seems unimpeachable. Thus, by reference to his latest report, above referred to, we find that in one series of experiments sixteen successive cultures were made during a period of twelve months, the original material being obtained from a cavity in a phthisical lung. Seventeen guinea-pigs were inoculated with the sixteenth culture, and all became tuberculous and died within six weeks. In another experiment four guinea-pigs were inoculated successfully with the twenty-sixth culture, the original material having been obtained from a human lung eighteen months previously. These examples represent but a small portion of the experimental evidence recorded in the report referred to, and the writer confesses that since he has become familiar with this evidence the last remnant of scepticism has been removed from his mind, and he now recognizes not only that tuberculosis is an infectious disease—a fact which had been prettly well demonstrated prior to Koch's discovery, and which I have repeatedly verified by inoculation experiments with phthisical sputum—but also that it is a parasitic disease, due to the presence in the body of an infected animal of the *Bacillus tuberculosis.*

This brings us to the question of the *modus operandi* of the bacillus in producing the infectious disease, tuberculosis. Does it act simply as a mechanical irritant, as maintained by Formad, of Philadelphia? and may it be replaced by other non-living mechanical irritants, as he claims to have demonstrated? or does the pathogenic power of the bacillus depend upon specific physiological characters peculiar to it?

By referring to the extract from a previous paper, quoted on page 17, it will be seen that two years ago the writer was inclined to favor the first mentioned view, inasmuch as it seemed to be supported by a considerable amount of experimental evidence, and because other experimenters—Klebs and Toussaint—had claimed to produce tuberculosis by inoculations with pure cultures of a different micro-organism. But to-day I feel compelled to admit that experiments made prior to the discovery of Koch's bacillus, especially when these were made in laboratories long in use for various pathological researches, can be accorded but little value on account of the great liability to accidental contamination of material used for inoculation experiments, or the subsequent infection of animals experimented upon through the wound made in these experiments. We now know that such experiments can have no scientific value in the absence of special precautions to prevent such accidental inoculation, which precaution no one thought of taking prior to the discovery of the tubercle bacillus.

But since this famous discovery was first announced, Dr. Formad, of Philadelphia, has repeatedly and emphatically declared that he is able to produce tuberculosis in rabbits, and in other animals, by injecting into the cavity of the abdomen, finely powdered inorganic material, such as glass, or ultramarine blue. This statement, coming from a pathologist of Dr. Formad's reputation, has had considerable weight with the writer, notwithstanding the fact that a detailed account of the experiments upon which it is founded has not yet been published. Being, then, still in doubt with reference to this important point, I determined, soon after the meeting of the American Medical Association in Washington, in May last, to repeat Dr. Formad's experiments with such precautions as would insure the exclusion to tubercle bacilli, and thus render it certain if a positive result was obtained that it was due solely to the inorganic particles introduced and not to accidental contamination of the material injected.

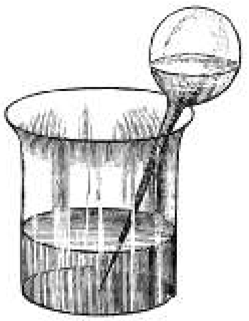
The main object of the present paper is to give an account of these experiments, which my assignment to duty in Baltimore, in June last, enabled me to carry out without delay, and with the co-operation of a competent pathologist, whose valuable assistance I hereby acknowledge, and whose notes relating to the pathological results of the injections made are embodied in the present paper. I am also indebted to Dr. Councilman for facilities for keeping my rabbits in the country under such circumstances as seemed to preclude the possibility of accidental inoculation with tubercle bacilli. The biological laboratory of Johns Hopkins University, where I have been engaged in other experimental work during the past summer, is a new building, and the animals might, perhaps, as well have been kept in it, an arrangement which would have been decidedly more convenient. But to avoid all possibility of accidental contamination the rabbits purchased especially for the experiment—fifteen in number—were sent directly to Dr. Councilman's home in the country, about eight miles from Baltimore, and were there placed in the loft of a storehouse, which had not previously been used for any similar purpose.

I was particularly desirous that the experiments should be made in a way which would be satisfactory to my friend, Dr. Formad, so that in case of a negative result the criticism might not be made that they were not properly done, and that a different mode of operating would have insured a different result. I accordingly invited Dr. Formad to assist in making the experiment, and he kindly came from Philadelphia, on a day appointed, for this purpose. Dr. Councilman, of Baltimore, was also present when the injections were made. The powdered glass used in the experiments was prepared by Dr. Formad, and the quantity of this, and of the marine blue, to be injected into each rabbit was determined by him. I was somewhat surprised at the considerable quantity of this material which Dr. Formad insisted upon using, for I had previously received the impression that in his experiments each particle served as a nucleus for a tubercle nodule, and consequently that but a small quantity of the finely divided inorganic material would be required in order to obtain a sufficiently characteristic result. The amount used for each injection must have considerably exceeded a drachm, and I should judge came nearer two drachms, although, as it was not weighed, I cannot speak more definitely as to the exact quantity. It was a matter of astonishment to me that such an amount of irritating material could be introduced into the peritoneal cavity of a delicate animal like the rabbit without producing fatal peritonitis. The inflammation which did occur was of a conservative and chronic kind, as is shown by Dr. Councilman's post-mortem notes, and, with two or three exceptions, the animals continued in apparent good health up to the time when they were killed, and were then found to be in good condition, and in the case of young rabbits to have grown very considerably in size. I ascribe this to the fact that the material had been thoroughly sterilized by the method shortly to be detailed, and that, consequently, no septic complications occurred. Dr. Formad has informed me that in his own experiments about one-third of the animals operated upon died during the first week from septicæmia, and that a certain number of the survivors suffered an acute inflammation, attended with the formation of pus, and its subsequent discharge through an opening in the walls of the abdomen. It is evident that animals in this condition would be exposed to contract tuberculosis in an affected locality by inoculation through the open wound in the belly.

Dr. Formad's method, as described to me, consisted in first making an incision through the integument over the belly; in then plunging a trocar or canula into the cavity of the abdomen; and finally, in injecting the sterilized material through the canula with a syringe. The wound was then closed by one or more stitches. The dangers and possibilities of accidental infection attending this mode of operating were avoided in my experiments by adopting the following method, the special advantages of which were at once recognized by Dr. Formad.

The finely powdered glass, or ultramarine blue, suspended in water, was introduced into little glass flasks with a long neck, such as I constantly use in my culture experiments, and one of which is represented in the figure in process of being filled with fluid from the glass beaker. The details relating to the manufacture and filling of these little flasks are given in my work on "Bacteria," from which the figure is taken. For this experiment the flasks were made rather larger than usual, their capacity being about a fluidounce. After filling them to about one-third their capacity, the extremity of each was hermetically sealed in the flame of an alcohol lamp. The contents were then

Fig. 1.



sterilized by placing them, for an hour or more, in a water-bath maintained at a boiling temperature.

The sterilized contents of one of these flasks were introduced directly into the abdominal cavity of each rabbit operated upon without any exposure to the external atmosphere or contact with other apparatus. This was accomplished as follows: The capillary extremity was first passed through the flame of a lamp to destroy any germs adhering to its external surface; the point was then broken off with sterilized forceps, and was thrust through the walls of the abdomen. By passing the tube beneath the skin for a short distance, and then directing it perpendicularly through the walls of the abdomen, a valvular opening is made, which prevents the admission of air or the escape of fluid when the tube is withdrawn. In operating by this method upon adult rabbits it is necessary to make a button-hole aperture through the skin with scissors, but the slender glass tube may be thrust through the thin skin of a young rabbit without difficulty. The contents of a flask were injected into the peritoneal cavity of each rabbit by the application of heat to its bulbous extremity by means of an alcohol lamp. The expansion of the inclosed air quickly forced out the fluid contents with the inorganic particles in suspension, and by this simple device all of the difficulties attending the use of an ordinary syringe were at once disposed of.

The experiment was made on the 17th of June; and on the morning of that day, before going to Dr. Councilman's home in the country, four rabbits were injected at the laboratory, two with ultramarine blue, and two with glass. In the afternoon eight of the fifteen rabbits in the country were injected, four with blue and four with glass, the remaining seven being kept as *témoins*.

The rabbits injected at the laboratory were intended to test the question whether association with tuberculous animals would make a difference in the result, and a few days later other rabbits injected with sputum, containing the tubercle bacillus, were placed in the adjoining compartment, which was only separated from that in which they were kept by a coarse wire screen.

One of the four rabbits operated upon at the laboratory was much emaciated, and evidently not in good health. This animal died the following day. Another of these rabbits died five days later, probably from injury to the intestine by the point of the glass tube. On the 15th of July another of these laboratory rabbits died, and, upon post-mortem examination by Dr. Councilman, the blue pigment was found in the cavity of the abdomen in great quantity, free or encapsuled, and also in the lymphatics of the diaphragm in such quantity as to give them the appearance of having been artificially injected. One rabbit injected with blue died in the country on the 26th of June, and one injected with glass on the 22d.

of July. The post-mortem examinations were carefully made by Dr. Councilman.

The time fixed by Dr. Formad at the outset for terminating the experiment was two months, and at my invitation he again came to Baltimore on the 27th of August to assist at the post-mortem examination of the remaining rabbits, which I proposed to kill on that day. All of the rabbits from the country were brought to the laboratory in Baltimore on the morning of the appointed day, and two were killed and carefully examined by Drs. Formad and Councilman in my presence. One of them had been injected with the blue pigment and one with glass. Both were well nourished, and the injected material was in each case found in the cavity of the abdomen in great abundance, encapsuled in larger or smaller masses, and contained in the mesenteric glands, in the lymphatics, etc.

A more exact account of the distribution of this material, and of the pathological appearances which had resulted from its presence, will be found in Dr. Councilman's notes, which he has kindly given me for publication in connection with my own account of the experiment. As these rabbits presented no evidence whatever of tuberculosis, those still remaining were, at Dr. Formad's suggestion, kept for another month. But, at my request, another rabbit, which had been inoculated subcutaneously with tuberculous sputum ten days after the experiment with inorganic material, was killed and examined. This animal was found to have typical tuberculosis of the lungs, and the presence of Koch's bacillus was demonstrated by Ehrlich's method, by spreading upon thin glass covers material from a caseous axillary gland, and also from a crushed tubercle nodule from the lungs.

One month later the remaining rabbits injected on the 17th of June were killed and carefully examined by Dr. Councilman and myself. They were all well nourished, and none of them presented any evidence of tuberculosis, the lungs and liver being normal in appearance, with the exception that upon the surface of the liver of a rabbit injected with glass there were small fibrous nodules containing this material. In the mean time I had killed another rabbit inoculated with sputum on the 27th of June, and, as before, found it to have unmistakable tuberculosis of the lungs. A third rabbit inoculated with sputum at the same time was killed a few days later, and it also had transparent nodules scattered through the lungs in which the presence of the bacillus tuberculosis was demonstrated.

It is unnecessary to say that this experiment gives no support whatever to the claim that tuberculosis may be induced by injecting into the abdominal cavity of rabbits finely powdered inorganic particles, or to the view that the tubercle bacillus induces tuberculosis by acting simply as a mechanical irritant.

Indeed this view is directly opposed by a vast amount of negative evidence familiar to pathologists, but which has not heretofore received the attention to which it is entitled. It is well known that the lungs of healthy adults contain a great number of inorganic particles, which find their way to the air cells with the inspired air and become fixed in the tissues in such quantity as to cause a dark-colored, mottled appearance upon post-mortem section. These particles consist for the most part of minute angular fragments of some form of carbon, and from their size and angular form it would seem that they should be more potent as mechanical irritants than the minute tubercle bacillus. I am informed that in Europe the lungs of men who have been employed in certain glass or porcelain works are found to contain innumerable angular fragments of this kind of material.

Moreover we have a form of consumption of the lung which is not due to tuberculosis and which is directly traceable to the inhalation of inorganic particles in large quantity. This disease has received different names, depending upon the special occupation which is the cause of its development. Thus at Wheeling, W. Va., where it is of frequent occurrence among those employed in the large nail mills in that city, it has received the name of "nailor's consumption." It is recognized by pathologists as being at the outset an interstitial pneumonia, and in the end it corresponds with what is known as fibroid phthisis. Quite recently my friend Dr. Jas. E. Reeves, of Wheeling, has examined numerous specimens of sputum from several victims of this disease, with reference to the presence of the tubercle bacillus. In no case has he been able to find it, although he is quite skilful in preparing specimens showing the bacillus in material which contain it, as I can testify, having recently seen some very beautiful preparations which he has mounted.

Even were it the case that inorganic particles deposited in the lungs may give rise to nodules anatomically identical with those found in the infectious disease tuberculosis, it would be necessary to admit that these are only pseudo-tubercles unless it can be shown that they undergo caseous degeneration and give rise to an extension of the tuberculous disease by auto-infection.

DR. COUNCILMAN'S REPORT.—At Dr. Sternberg's request I undertook the examination of the rabbits injected with various inert substances in presence of Dr. Formad on the 17th of June last.

The pathological changes produced differed somewhat in those injected with blue from those where glass was used, the differences, however, in the individual cases of each were slight. Four rabbits were examined that had been injected with blue. One of these died June 26th. In this rabbit a quantity of serum slightly tinged with blood was found in the abdominal cavity, there was a slight fibrinous exudation with tender adhesions of the viscera in a few places. The entire peritoneum was slightly reddened and the bloodvessels injected. There was no pus and no appearance of a purulent inflammation. The lungs and other viscera were healthy. Large quantities of the blue pigment were found, part of which was lying free in the cavity, part was enveloped in the fibrinous exudation or inclosed in the adhesions. The other three rabbits were killed later.

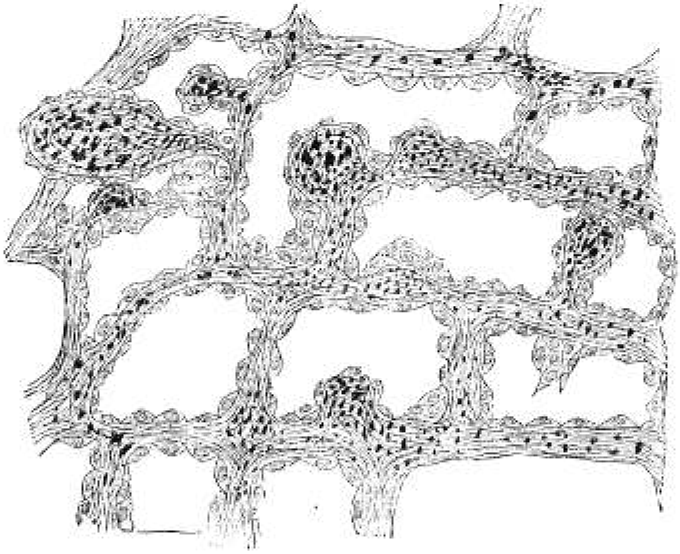
On opening the abdominal cavity the blue pigment was found pretty well distributed over the entire peritoneal surface. In the mesentery a few small blue nodules were found, and streaks of blue along the mesenteric vessels. Circumscribed blue nodules from the size of a pin's head up to that of a pea were also found at various places on the serous surface of the intestines, on the surface of the liver, and on the spleen. In one rabbit, on the posterior surface of the peritoneal cavity, there were numerous small villous-like projections intensely stained with blue, these were evidently similar to the papillary projections so often found on the human peritoneum. There were some adhesions between the various viscera, principally between the colon and cæcum, all of which adhesions were of an intensely blue color. The mesenteric glands were enlarged and injected with pigment, the lymphatics of the diaphragm were marked out in blue, and the lymph glands in the anterior mediastinum were also colored. A slight amount of blue was found beneath the skin at the point of injection. Lungs, liver, spleen, kidneys, and intestines healthy save for the common parasites so often found in the liver.

An examination of the blue nodules on the liver with a hand lens showed around each a whitish band of connective tissue. On sections of the nodules being made, stained in carmine and mounted in glycerine or balsam, they were seen to be composed of masses of pigment inclosed in well-formed connective tissue. The smaller nodules were simply encapsuled; in most of the larger there was not only a layer of connective tissue over the whole nodule but bands ran through the pigment dividing it into smaller masses. The adhesions were found to consist of dense connective tissue which inclosed in its fibres large quantities of pigment.

The two layers of the omentum were generally adherent; in some places, however, they could be easily separated. The membrane was stained in carmine and examined in glycerine. The microscopic appearances were extremely interesting, and showed very clearly the effect of continued irritation on a serous membrane (Fig. 2).

The endothelial cells, as seen on the edges of the trabeculæ, were slightly swollen and more granular than in the normal. At numerous places two or more layers of cells which often contained pigment granules were seen. At various places there were bud-like projections from the trabeculæ which contained large quantities of pigment, and were covered with endothelium. Every change could be seen from a mere thickening

Fig. 2.



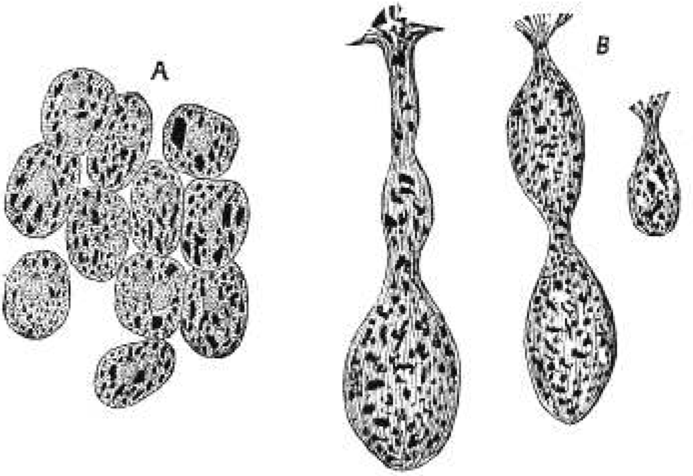
Omentum of rabbit after the injection of Berlin blue into the abdominal cavity.

of a trabeculum to a long process only connected by a narrow stalk. Pigment was irregularly distributed throughout the fibrous tissue of the trabeculæ.

An examination of the peritoneal surface elsewhere showed that the pigment was mostly distributed in the lymph spaces and lymphatics beneath the endothelium. Of its easy entrance into these vessels the injection of the various lymph glands gives abundant proof. The endothelial cells were generally free from pigment; only in a few places were found groups of large granular cells (Fig. 3 *A*) which contained it in large quantities. These cells evidently corresponded with the so-called germinating endothelium described by Klein and others. At numerous places all over the peritoneum, sometimes growing from the midst of a group of pigment-containing endothelial cells, were long villous-like formations of connective tissue (Fig. 3 *B*) with rounded ends. These contained abundant pigment, and most probably represented adhesions which had become elongated and finally broken by traction (Fig. 3).

In the rabbits that had been injected with glass the adhesions were more numerous and extensive than in the others. Numerous nodules of various sizes from the head of a pin up to that of a bean were found at various places. In one rabbit a large whitish mass was found at the point of injection as large as the end of the thumb. These masses were of a whitish color, and on section a soft mass could be squeezed out of them which could be rubbed between the fingers. An indistinct division

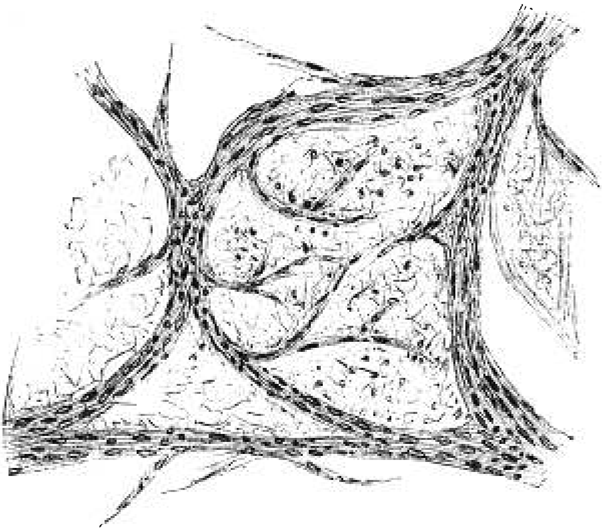
Fig. 3.



From same rabbit as Fig 2. *A*, germinating endothelium containing blue pigment. *B*, papillary connective tissue formations.

of the mass could be seen on the surface of the section. In the omentum and other places on the peritoneum small white points could also be seen. No lymph glands were enlarged. The larger nodules presented somewhat the appearance of conglomerate tubercles, and the substance squeezed out of them might, without even a superficial microscopic examination, be taken for a caseous mass. In like manner the small nodules in the omentum might have been taken for miliary tubercles but they were rather too transparent. Microscopic examination set all doubts at rest. The large nodules were composed of masses of glass inclosed in connective tissue. This not only inclosed the whole nodule but large bands of it penetrated between the glass dividing it up into small areas. From these larger bands smaller ones were again given off (Fig. 4). Between these bands nothing but minute fragments of glass and a few cells were found. The bands of connective tissue contained numerous bloodvessels. The smaller nodules were found where only a small amount of glass was present. Sometimes but a slight nuclear increase would be found around one or two bits of glass; at other times the glass would be inclosed in a small mass of connective tissue very rich in cells. At no place was any glass taken up by the tissue or found in the lymphatics—in striking contrast to what was found when the blue was used for injection. The adhesions were composed of newly-formed connective tissue rich in cells, and contained numerous small masses of glass inclosed in a capsule. There was also a good deal of the glass irregularly distributed in the connective tissue.

Fig. 4.



Section of nodule from the serous surface of intestine after the injection of powdered glass into the abdominal cavity.

There were many examinations made, both when the rabbits were killed and afterwards, of the nodules produced from the blue and the glass with regard to the presence of tubercle bacilli, but with, it is needless to say, negative results. The organs in which no changes were perceptible to the unaided eye were carefully examined microscopically, numerous sections of lungs, liver, spleen, and kidneys were made, but no pathological changes discovered. In no instance was any caseation found, and there were no nodules which had even the anatomical structure of tubercles—the so-called pseudo-tubercles.

Three rabbits were examined that had been injected with tubercular sputum. In two of these the most typical tuberculosis was produced. There was a large caseous mass at the point of injection, the axillary glands were caseous, and there were innumerable caseous nodules in the lungs, liver, and elsewhere. In one there was no caseation at the point of injection nor were the lymph glands affected. The lungs, however, contained innumerable grayish semi-transparent nodules, some single, others conglomerate. Examinations were made from all cases, and tubercle bacilli were found in every instance both in the nodules in internal organs, in the caseous mass at the point of injection, and in the caseous lymph glands.

Postscript.—The following interesting letter from Dr. Reeves, relating to a form of consumption of the lung induced by mechanical irritation, but

which is evidently not tubercular, was not received until after the manuscript of the above paper had left my hands. I therefore append it as a postscript.
G. M. S.

WHEELING, W. VA., October 26, 1884.

DEAR DR. STERNBERG: I promised you at St. Louis week before last, that, as soon as possible after my return home, I would give you a brief statement of my observations concerning so-called "Nailers' Consumption," a disease which kills about 80 out of every 100 nailers in this community before they reach the age ot 55 years.

In "The Wheeling Iron and Nail District" there are 10 iron and nail mills, employing in the aggregate not less than 7000 persons. Of these, 400 are nailers, each of whom has charge of two, three, or four machines, according to his experience and skill in making nails; and the greater part of his time while at work is occupied in grinding his bits or knives. While engaged in such work at the rapidly-revolving grindstones his hair, beard, and clothing soon become well powdered with the fine particles of sand and steel which float in his breathing space and choke his bronchial tubes.

Nine out of ten of these operatives suffer from hacking cough, accompanied with dark-colored expectoration, and dyspnœa, within the first year after they commence grinding; and the progression of the pulmonary symptoms is a gradual descent until the vital spark is extinguished. In other words, there is at first a bronchitis; next, a chronic interstitial pneumonia and induration of the lung tissue; next, softening and excavation, occasional hæmoptysis, muco-purulent expectoration, wasting of flesh, hectic, and night-sweats.

Several years ago I carefully examined 136 nailers, according to the scope of the printed schedule herewith inclosed, and out of that number found only one whom I regarded entirely free from pulmonary disease. In all of the others there was more or less dulness on percussion, bronchial breathing, increased vocal resonance, and conduction of the cardiac sounds.

The *post-mortem* appearances are quite uniform. The pigmentation of the usually contracted lungs is in proportion to the number of years the subject has spent in the mills. In some instances the lungs are as black as if they had been stained with ink.

The induration of lung tissue includes fibrous deposits, varying in size from small nodules to large masses, and, in resistance to the knife, resembles cartilage. In some instances such nodules or masses appear really gritty. The bronchi are dilated, and the bronchial glands are enlarged and hardened.

Pleural adhesions are very common. In one instance the pleural surface was studded with calcareous deposit in the form of very thin plates. Now and then a case will be met with where the lungs are also the seat of tuberculosis; but, in such instances, I doubt not, the family history, if questioned, will show tuberculous tendency.

During the last several months I have made frequent careful microscopic examinations of the sputa from subjects of "Nailers' Consumption," in search for *Koch's bacillus*, but thus far with negative result, notwithstanding the specimens examined represented the first, middle, and last stages of the disease—in one case even so late as a few days before the death of the patient. But, no doubt, I shall yet find the *tubercle bacillus* in the sputum from such a patient for the reason just mentioned, in describing the *post-mortem* appearances, namely, the lungs may also show tuberculous deposit.

A few weeks ago I picked up, from the sidewalk or pavement near my residence, a portion of a sputum that had been expelled by some passer-by, which furnished one of the best mounts I possess of *Koch's tubercle bacillus*. This fact points to a possibility needless here to mention.

Very truly yours,
JAMES E. REEVES.